Summary of Efficacy Data for Isopropyl and Ethyl Alcohol

Healthcare Personnel Handwash Studies

1). The Evaluation of the Efficacy of Two Alcohol Handrubs and One Triclosan-Containing Handwash Product in a Healthcare Personnel Handwash Procedure Project No. 02-121277-106

A four arm study was conducted using three (3) g of a foamed 62% ethyl alcohol handrub (EtOH), five (5) mL of a 0.5 % triclosan handwash product, five (5) mL of a 4% chlorhexidine gluconate handwash (CHG) product and five (5) mL of a 63% isopropyl alcohol (IPA) handrub.

The objective of the study was to demonstrate the antibacterial effectiveness of the products when tested under the conditions of the Food and Drug Administration (FDA) Tentative Final Monograph (Vol. 59, No. 116, June 17, 1994, FR 31402) as shown by at least a two (2) $\log_{10}$ reduction of the indicator organism, *Serratia marcesens* (ATCC 14756) within five (5) minutes after the first hand treatment with the test articles and at least a (3) $\log_{10}$ reduction within five (5) minutes after the tenth treatment. Twenty-four (24) subjects were selected to participate in the study, six (6) subjects in each arm.

The subject population for the test phase was defined as twenty-four (24) subjects either male or female no less than eighteen (18) years of age. The subject population for the neutralization assay phase was defined as four (4) subjects either male or female no less than eighteen (18) years of age.

Fifty-six (56) subjects were enrolled in the pre-test conditioning phase. Twenty-four (24) subjects, ten (10) males and fourteen (14) females, who met the study criteria were enrolled in the test phase and completed the study.

Thirty-two (32) subjects were excluded or withdrew from the study. Seventeen (17) subjects withdrew for personal reasons. Nine (9) subjects were excluded due to lack of compliance with the protocol. Six (6) subjects were extra.

The IPA product showed a 3.86 $\log_{10}$ reduction in numbers of the indicator organism within five (5) minutes of the first hand treatment and a 2.83 $\log_{10}$ reduction within five (5) minutes of the tenth hand treatment. The EtOH product showed a 2.87 $\log_{10}$ reduction after the first hand treatment and a 1.29 $\log_{10}$ reduction after the tenth hand treatment. The CHG product showed a 2.65 $\log_{10}$ reduction after the first hand treatment and a 3.96 $\log_{10}$ reduction after the tenth hand treatment. Table I depicts the results from this study.

Table I

Product	1st Hand Treatment Log_{10} Reduction	3rd Hand Treatment Log_{10} Reduction	7th Hand Treatment Log_{10} Reduction	10th Hand Treatment Log_{10} Reduction
EtOH	2.87	1.64	1.38	1.29
IPA	3.86	2.75	2.82	2.82
CHG	2.65	3.21	4.0	3.96

The study was completed and a final report was issued on June 24, 2003.

2). **The Evaluation of the Antimicrobial Efficacy of Two Alcohol Hand Rubs, One Triclosan-Containing Handwash Product, and One Reference Product Using the ASTM Standard Test Method for Evaluation of Health Care Personnel Handwash Formulations (E 1174-00) Project No. 030114-101**

A four arm study was conducted using three (3) g of a foamed 62% ethyl alcohol handrub (EtOH), five (5) mL of a 0.5 % triclosan handwash product, five (5) mL of a 4% chlorhexidine gluconate handwash (CHG) product and five (5) mL of a 63% isopropyl alcohol handrub (IPA).

The purpose of this study was to determine the antimicrobial effectiveness of the test articles when tested under the conditions of the ASTM Standard Test Method for Evaluation of Health Care Personnel Handwash Formulations (E 1174-00). The study objective was that at least a two (2) log_{10} reduction of an indicator organism *Serratia marcesens* (ATCC No. 14756) be achieved within five (5) minutes after the first hand treatment with the test articles and at least a three (3) log_{10} reduction after the eleventh hand treatment. Twenty-four (24) subjects, six (6) subjects in each arm, were selected to participate in the study.

The subject population for the test phase was defined as twenty-four (24) subjects either male or female no less than eighteen (18) years of age. The subject population for the neutralization assay phase was defined as four (4) subjects either male or female no less than eighteen (18) years of age.

Forty-eight (48) overtly healthy subjects over the age of eighteen (18), but under the age of seventy (70) were admitted into the study. Twenty-four (24) subjects completed the study. Of the twenty-four (24) subjects who completed the study, four (4) were male, twenty (20) were female, one (1) was Hispanic, one (1) was Caucasian/African-American, and twenty-two (22) were Caucasian.

Twenty (20) subjects were excluded or withdrew from the study. Ten (10) subjects withdrew for personal reasons and ten (10) subjects were excluded due to inability to meet the inclusion criteria.

The IPA product showed a 3.69 $\log_{10}$ reduction in numbers of the indicator organism within five minutes of the first hand treatment and a 3.24 $\log_{10}$ reduction within five (5) minutes of the eleventh wash. The EtOH product and the CHG product showed a 2.61 $\log_{10}$ reduction and a 2.62 $\log_{10}$ reduction after the first hand treatment respectively. At the end of the eleventh hand treatment, the EtOH showed a 2.39 $\log_{10}$ reduction and the CHG product showed a 3.56 $\log_{10}$ reduction. Table II depicts the results from the study.

Table II

Product	**1st Hand Treatment $\log_{10}$ Reduction**	**11th Hand Treatment $\log_{10}$ Reduction**
EtOH	2.61	2.39
IPA	3.69	3.24
CHG	2.62	3.56

A final report has not been issued for this study to date. The protocol of the study is attached.

Table III compares the results of the $\log_{10}$ reduction from baseline obtained with the IPA product used in a TFM test method versus an ASTM test method for evaluating health care personnel handwash formulations.

Table III

IPA	**Baseline Counts**	**1st Hand Treatment $\log_{10}$ Reduction**	**10th Hand Treatment $\log_{10}$ Reduction**	**11th Hand Treatment $\log_{10}$ Reduction**
TFM Test Method	8.90	3.86	2.82	
ASTM Test Method	9.53	3.69		3.24

In both studies, there is a decline from the first hand application to the tenth and eleventh hand applications. The downward trend from first to last (10th) hand applications is more dramatic in the TFM test method versus the ASTM test method. The decrease in log reductions from wash one (1) to wash ten (10) is a phenomenon observed in other published studies[1] with leave-on alcohol-based products. This trend is reproducible and influenced by test methodology and its design for wash-off products. Further investigations have been initiated in order to minimize this methodology-based artifact.

1 Paulson DS, Fendler EJ, Dolan MJ, Williams RA. A close look at alcohol gel as an antimicrobial sanitizing agent AJIC Am J Infect Control 1999; 27:332-8. (Attached)

Surgical Scrub Study

An Evaluation of an Isopropyl Alcohol Handrub and a CHG Scrub for Antimicrobial Effectiveness and Substantivity in the Surgical Scrub Using Normal Skin Flora Project No. 03-121432-106

A three arm study was conducted using a 63% isopropyl alcohol (IPA) handrub and a 4% chlorhexidine gluconate (CHG) handwash product.

The objective of the study was to determine the antibacterial effectiveness of the test product used in a surgical scrub procedure when tested under the conditions of the Food and Drug Administration (FDA) Tentative Final Monograph (Vol. 59, No. 116, June 17, 1994, FR 31402) as shown as shown by a reduction in resident bacteria by at least a one (1) $\log_{10}$ reduction on each hand within one (1) minute of product use on the first day, a two (2) $\log_{10}$ reduction of the microbial flora on each hand within one (1) minute of the first product use on the second day and a three (3) $\log_{10}$ reduction of the microbial flora on each hand within one (1) of product use on the fifth day when compared to the established baseline. Regrowth was measured to determine whether the bacterial cell count on each hand did not exceed baseline.

The IPA product was used in two arms of the study. In Arm A, subjects applied the IPA product twice. Five (5) mL of the IPA product was dispensed in the first application. Subjects rubbed the IPA product into the hands and forearms until dry. In the second application, two and a half (2.5) mL of the IPA product was dispensed and the subjects rubbed into the hands until dry.

In Arm B, subjects applied the IPA product three times. In the first application, five (5) mL of product was dispensed and rubbed into the hands and forearms until dry, in the second application two and a half (2.5) mL of product was dispensed and rubbed into the hands until dry and in the third application, another two and a half (2.5) mL of product was dispensed and rubbed into the hands until dry.

In Arm C, the CHG handwash product was used according to the label directions for a surgical scrub.

The subject population for the test phase was defined as twenty-four (24) subjects either male or female no less than eighteen (18) years of age. The subject population for the neutralization assay phase was defined as six (6) subjects either male or female no less than eighteen (18) years of age.

The results of the study are depicted in Table IV.

Table IV

	IPA (Arm A)	IPA (Arm B)	CHG
Day 1			
0 Hour	2.60	2.85	1.74
6 Hour	2.42	2.75	1.47
Day 2			
0 Hour	2.65	2.98	2.46
6 Hour	2.78	2.95	2.26
Day 5			
0 Hour	1.71	2.05	2.94
6 Hour	1.64	1.94	3.24

The IPA product met the TFM criteria for a surgical scrub in Arm A on Days one (1) and two (2) at zero (0) hour with results of 2.60 $\log_{10}$ reduction and 2.65 $\log_{10}$ reduction respectively. In Arm A, IPA did not allow regrowth of the normal resident flora to exceed baseline counts on Days one (1), two (2), and five (5). In Arm B, the IPA product met the TFM criteria for Days one (1) and two (2) at zero (0) hour with results of 2.85 $\log_{10}$ reduction and 2.98 $\log_{10}$ reduction respectively. The IPA results are comparable to the 4% CHG product on Days one (1) (1.74 $\log_{10}$ reduction) and two (2) (2.46 $\log_{10}$ reduction). The 4 % CHG product marginally met the criteria for Day five (5).

The results obtained with IPA in the 2003 surgical scrub study are comparable to results obtained in a surgical scrub study conducted with an ethyl alcohol (EtOH) product. Both actives showed substantial log reductions from baseline and persistent activity with no return to baseline after six (6) hours. The results of the EtOH product in a surgical scrub were previously filed to the Docket by ConvaTec in 1995. In that study, a 62% EtOH product showed results on Days one (1), two (2), and five (5) at zero (0) hour of 1.83 $\log_{10}$ reduction, 1.98 $\log_{10}$ reduction, and 2.01 $\log_{10}$ reduction respectively. The EtOH product did not allow regrowth to exceed baseline counts. Table V depicts the comparison between the ethyl alcohol product tested in 1995 and the IPA product tested in 2003.

Table V

	EtOH (1995)	IPA Arm A (2003)	IPA Arm B (2003)
Day 1			
0 Hour	1.83	2.60	2.85
6 Hour	1.11	2.42	2.75
Day 2			
0 Hour	1.98	2.65	2.98
6 Hour	1.52	2.78	2.95
Day 5			
0 Hour	2.01	1.71	2.05
6 Hour	1.96	1.64	1.94

A comparison of the results show that 63% IPA when properly formulated, provides comparable efficacy to 62% EtOH in a surgical scrub application.

A final report has not been issued for this study to date. The protocol for the study is attached.

Ethyl Alcohol

Surgical Scrub Study

An Evaluation of an Ethyl Alcohol Handrub and a CHG Scrub for Antimicrobial Effectivenss and Substantivity in the Surgical Scrub Using Normal Skin Flora
Project No. 02-121276-106

A three arm study was conducted using a 62% ethyl alcohol (EtOH) handrub and a 4% chlorhexidine gluconate (CHG) handwash product.

The objective of the study was to determine the antibacterial effectiveness of the test product used in a surgical scrub procedure when tested under the conditions of the Food and Drug Administration (FDA) Tentative Final Monograph (Vol. 59, No. 116, June 17, 1994, FR 31402) as shown as shown by a reduction in resident bacteria by at least a one (1) $\log_{10}$ reduction on each hand within one (1) minute of product use on the first day, a two (2) $\log_{10}$ reduction of the microbial flora on each hand within one (1) minute of the first product use on the second day and a three (3) $\log_{10}$ reduction of the microbial flora on each hand within one (1) of product use on the fifth day when compared to the established baseline. Regrowth was measured to determine whether the bacterial cell count on each hand did not exceed baseline.

The EtOH product was used in two arms of the study. In Arm A, subjects applied the EtOH product twice. Five (5) g of the EtOH product was dispensed in the first application. Subjects rubbed the product into the hands and forearms until dry. In the second application, two and a half (2.5) g of the product was dispensed and the subjects rubbed into the hands until dry.

In Arm B, subjects applied the EtOH product three times. In the first application, five (5) g of product was dispensed and rubbed into the hands and forearms until dry, in the second application two and a half (2.5) g of product was dispensed and rubbed into the hands until dry and in the third application, another two and a half (2.5) g of product was dispensed and rubbed into the hands until dry.

In Arm C, the CHG handwash product was used according to the label directions for a surgical scrub.

The subject population for the test phase was defined as twenty-four (24) subjects either male or female no less than eighteen (18) years of age. The subject population for the neutralization assay phase was defined as six (6) subjects either male or female no less than eighteen (18) years of age.

The results of the study are depicted in Table VI.

Table VI

	EtOH (Arm A)	EtOH (Arm B)	CHG
Day 1			
0 Hour	2.75	2.87	1.86
6 Hour	2.81	2.94	0.64
Day 2			
0 Hour	3.21	3.07	2.71
6 Hour	3.19	3.05	1.20
Day 5			
0 Hour	3.02	3.12	3.21
6 Hour	3.13	2.87	1.98

The EtOH product met the TFM criteria for a surgical scrub in Arm A on Days one (1), two (2), and five (5) at zero (0) hour with results of 2.75 $\log_{10}$ reduction, 3.21 $\log_{10}$ reduction, and 3.02 $\log_{10}$ reduction respectively. In Arm A, EtOH did not allow regrowth of the normal resident flora to exceed baseline counts on Days one (1), two (2), and five (5). In Arm B, the EtOH product met the TFM criteria for Days one (1), two (2), and five (5) at zero (0) hour with results of 2.87 $\log_{10}$ reduction, 3.07 $\log_{10}$ reduction, and 3.12 $\log_{10}$ reduction respectively. Again, in Arm B, the EtOH product did not allow regrowth to exceed baseline counts. The EtOH results are comparable to the 4% CHG product on Day one (1) (1.86 $\log_{10}$ reduction), Day two (2) (2.71 $\log_{10}$ reduction), and Day five (5) (3.21 $\log_{10}$ reduction).

A final report has not been issued for this study to date. The protocol of the study is attached.